The Root Cause of Nicotine Market Failure and Implications

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1 Executive Summary

The current nicotine market represents a market failure. It is deeply flawed in that the most consumer-satisfying product in the short-term is the most harmful to health in the long-term, which drives massive premature loss of life and contributes to human suffering, in addition to increasing costs on society such as excess medical expenditures and loss of productivity.

Smoking of combustible tobacco products is responsible for almost all tobacco-related harm. In fact, CDC does not even publish an estimate of premature deaths caused by tobacco products other than cigarettes. To prevent unnecessary suffering because of combustible tobacco-related illness and disease, FDA should ensure that newly deemed noncombustible sources of nicotine are not subject to stricter regulation standards than tobacco products that burn.

To that end, we recommend that FDA vary the periods of exercising enforcement discretion of requiring product marketing applications depending on whether the newly deemed products involve combustion to use them or not. We recommend that FDA deem products that burn as outlined in the proposed rule. For products that do not burn, we recommend that FDA change the grandfather date to match the effective date of the final rule and extend the period requiring companies to submit a pre-market tobacco products application (PMTA) to 72 months (six years).

2 Disclosures

We write as public health professionals who have worked on tobacco and public health issues with the federal government, academia, health voluntary organizations, and as consultants to the private sector. In the past three years, our consulting firm has provided services for a range of companies, including for GlaxoSmithKline Consumer Healthcare on their stop-smoking medications (Nicorette and NicoDermCQ in the US), for NJOY, Inc., a developer and marketer of electronic nicotine delivery systems, and since February 2015, for Reynolds American, Inc. on tobacco harm minimization. Our work for RAI focuses on products, regulations, and policies related to smoking cessation and harm minimization; we do not work on combustible conventional cigarettes. Some of us (JMP, JGG, SS) also are members in a limited liability corporation that owns intellectual property for an as-yet not-commercialized nicotine gum an option for which has been acquired by Niconovum, a subsidiary of RAI. These comments, however, reflect our own views exclusively and with them we are representing no one but the authors above.

3 Analysis

In this brief paper, we argue that the root cause of the flawed nicotine market is information asymmetry, exacerbated by and interacting with specific product characteristics that make the most consumer-satisfying product in the short-term the most harmful to health in the long-term. Based on this analysis, we then propose considerations that should help policymakers, including the FDA, select efficient and appropriate alternative regulatory pathways consistent with the authority granted to the FDA by Congress to address this problem.

We see two realities that fundamentally shape the nicotine market and are the root cause of the market failure:

1. Consumers do not have adequate correct information to make choices consistent with their interests. Many tobacco users believe that nicotine is harmful on its own when it is clear that nicotine is not what makes combustible tobacco deadly, and it is generally considered safe in non-pregnant adults. This is a form of information asymmetry, but with the variation that public health experts, in addition to tobacco producers, typically have more information than the overwhelming majority of consumers – more details at this section: Evidence Summary: Consumers lack necessary information, and much of what they *think* they know is wrong. We do not seek to review or resolve the issue as to whether or not smokers make accurate assessments of the *absolute* risks of smoking but attempt to focus on the more salient issue of smokers' understanding of the *relative* risks across nicotine products; and

2. The massive distortion caused by combustion cigarettes being both the most addictive (and thus most choice-eroding) and lethal nicotine delivery systems.

Our position is supported by scientific and public health literature (Warner et al, 1997, Sumner, 2003 and 2005, Chaloupka, Warner & Sweanor 2015b; Viscusi, Smoking – Making the Risky Decision), but the logic of applying market-based analysis and tools has received relatively little attention within the body of tobacco control research and recommendations.

One implication of limited attention to this line of reasoning is that much of the existing efforts to address the harms of smoking address the *consequences* of the underlying market failure rather than the root cause itself. Broadly, especially over the past 20 years, policies and interventions have predominantly focused on restrictions and discouraging use of "tobacco."

For example, the World Health Organization recommends increasing excise taxes on all tobacco products at comparable levels to advance the goal of "…minimizing opportunities for substitution." This mindset pervades other pillars of tobacco control, such as restrictions on where smokers (and increasingly vapers) can use their products, and health education campaigns that seek to conflate the use of e-cigarettes with combustion cigarettes. In fact, the more obvious conclusion from this review is that if anything, existing policy and education interventions have the unintended consequence of reinforcing information asymmetry and possibly increasing harm, rather than ameliorating it.

As a result of this analysis, we would submit that government efforts to reduce the burden of premature death and chronic disease caused by combustible tobacco should be targeted to address the fact that most consumers do not understand the relative risks of different tobacco and nicotine products. This burden should be calibrated and targeted to address the root cause of market failure, particularly the first prong, not the resulting consequences of the market failure. The reason for the focus on the first prong is that the two factors in the root cause do not operate independently. If the first were

addressed, it would be much easier to minimize the impact of the second, yet addressing the second alone, without solving the first, would likely result in an array of costly and harmful unintended consequences.

Consistent with the priorities and preferences in EO 12866 and other policies, and as argued for in an array of policy publications by Sunstein, Thaler, and others, OIRA notes on page 5 of its primer for regulatory agencies when preparing their Regulatory Impact Analyses, regulations should consider:

> - *Market-oriented approaches rather than direct controls.* Agencies should consider market-oriented regulatory approaches that use economic incentives to achieve regulatory goals and that afford entities greater flexibility in compliance. Such approaches include fees, penalties, subsidies, marketable permits or offsets, changes in liability rules or property rights, and required bonds, insurance, or warranties. In the domain of environmental protection, for example, emissions trading may deserve careful consideration as an approach that might achieve the same gain at a significantly lower cost.
>
> ...
>
> - *Informational Measures.* If intervention is contemplated to address a market failure that arises from inadequate or asymmetric information or poor information processing, informational remedies will often be preferred. To the extent feasible, specific informational measures should be evaluated with reference to their benefits and costs.

We would urge that at a minimum any tobacco-product regulation meet these goals:

- First, do not make consumers' information deficit *worse*. As the summary below indicates, efforts that further demonize nicotine and distort its contribution to disease in the absence of smoke, either directly or indirectly, should be meticulously avoided.
- Second, explore, research, and implement efforts to reduce consumers' information deficit, specifically to highlight the massive differences in inherent toxicities between products that burn and products that do not. Given the history and extent of this problem, solving it is unlikely through any single effort—and it will take considerable time. These misperceptions have accumulated over decades. It is likely that some combination of public (bringing comparative enhanced credibility and authority) and private (contributing likely greater resources and the advances and refinements that market forces will drive) efforts will be most effective at addressing these issues.

Separately, but relatedly, we understand that FDA is in the process of evolving (or has evolved, for example, here and here) its approach to dealing with consumer surplus with tobacco product regulation. We agree with the arguments that as a result of a number of factors (see Chaloupka et al, 2015), cigarette smoking is not a rational choice and thus typical accounting for lost consumer surplus does not apply (or should be substantially discounted).

On the other hand, we would submit that consumption of very low risk tobacco or nicotine products does meet the expectations of rational choice and thus any regulatory actions that serve to decrease the adult use of products such as nicotine medications, low-nitrosamine snus, or vapor products, need to take into account consumer surplus.

4 Recommendation

While the scope of the deeming rule does not include opportunities to correct the information asymmetry, a deeming rule that places the same or higher regulatory burden on less harmful products will likely increase the negative population effects of information asymmetry. Conversely, a reasonable deeming rule can work to avoid making it worse and at least be consistent with the notion, embraced by FDA CTP leadership, that nicotine products present vastly different risk profiles and should not be treated equally.

We recommend that FDA vary its approach in regulating newly deemed tobacco products. For products that involve combustion, the grandfather date should remain the same and enforcement discretion would stop after 24 months, consistent with the proposed rule. For non-combusted tobacco products, we recommend that FDA change the grandfather date to the date of the final rule and extend the enforcement discretion period to 72 months (six years).

5 Proposed Edits, Based on Proposed Rule

In this section 5, we have suggested specific edits to language from the Proposed Rule.

5.1 Proposed §1100.3–Definitions Modifications

The definition in proposed § 1100.3 is a restatement of the statutory definition of "tobacco product" found in section 201(rr) of the FD&C Act. FDA proposes to ~~restate~~further refine the definition of ~~"~~"subcategories of 'tobacco product" in ~~two~~three parts: (1) ~~Tobacco~~ Combusted tobacco product means any product made or derived from tobacco that is intended to be combusted for human consumption, including any component, part, or accessory of a tobacco product (excluding raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product) ~~and (2~~(2) Non-combusted tobacco product means any product made or derived from tobacco that is intended for human consumption without combustion, including any component, part, or accessory of a tobacco product (excluding raw materials other than tobacco used in manufacturing a component, part, or accessory of a tobacco product) and (3) tobacco product does not mean an article that is a drug, device, or combination product as those terms are defined in the FD&C Act. We are repeating the statutory definition of "tobacco product" in this proposed rule for easy reference for readers of this regulation.

5.2 Proposed Regulatory Approach for Newly Deemed Tobacco Products

FDA also is soliciting comment on what FDA actions or regulatory approaches, if any, should be taken for proposed deemed tobacco products that are "new combusted tobacco products" or "new non-combusted tobacco products" under section 910(a)(1) of the FD&C Act. A new combusted tobacco product means "any combustible tobacco

product (including those products in test markets) that was not commercially marketed in the United States as of February 15, 2007; or any modification (including a change in design, any component, any part, or any constituent, including a smoke constituent, or in the content, delivery or form of nicotine, or any other additive or ingredient) of a tobacco product where the modified product was commercially marketed in the United States after February 15, 2007" (section 910(a)(1) of the FD&C Act). A new non-combusted tobacco product means "any non-combusted tobacco product that was not commercially marketed in the United States as of [the effective date of part 1100]." In general, a tobacco product manufacturer has three pathways for legally marketing a new tobacco product: (1) The manufacturer obtains an order under section 910(c)(1)(A)(i) (order after review of a premarket application) before the manufacturer introduces a new tobacco product into interstate commerce (section 910 of the FD&C Act); (2) the manufacturer obtains an order finding substantial equivalence under section 910(a)(2)(A) of the FD&C Act (order after review of a section 905(j) report) before the manufacturer introduces a new tobacco product into interstate commerce (section 910 of the FD&C Act); and (3) the manufacturer makes a request under § 1107.1 (21 CFR 1107.1) and obtains an exemption from the requirements related to substantial equivalence.5 Tobacco products (whether combusted or non-combusted) that were commercially marketed (other than for test marketing) in the United States as of February 15, 2007, are not "new tobacco products" subject to the premarket requirements, and FDA refers to these products as "grandfathered."~~Based~~"

Based on initial information FDA has gathered and received from industry, many tobacco products we are proposing to deem that are currently being sold may not be "grandfathered" tobacco products because many were not commercially marketed or modified until after February 15, 2007. We understand that this may be particularly true in the case of e-cigarettes and similar novel products. Moreover, new products that come on the market in the future would never be grandfathered tobacco products because they would be coming on the market after February 15, 2007. We do not believe that we have the authority to alter or amend this grandfathering date, which is set by statute. Therefore, FDA believes most proposed deemed tobacco products would be considered new tobacco products and would be required to obtain an order from FDA prior to marketing under one of the three pathways listed in section VIII.A.6. As stated in sections VIII.A.6.c and VIII.A.6.d, FDA is proposing a 24-month compliance policy for manufacturers of proposed deemed combusted tobacco products to submit marketing applications. FDA is proposing a 72-month compliance policy for manufacturers of proposed deemed non-combusted tobacco products to submit marketing applications. FDA does not intend to initiate enforcement action against products on the market for failing to have an FDA marketing authorization until 24 months following the effective date of the final rule. In addition, as described in section VIII.A.6.c, we intend to continue that compliance policy pending review of marketing applications if those applications are submitted within the 24 months after the final rule's effective date. We intend to work with industry to assist them in making submissions. We expect that our proposed approach, as discussed in this section, would help minimize disruption while FDA conducts its pre-market review. Further, we request comment on whether there are ways that we might provide additional flexibility with respect to PMTAs that would still be appropriately protective of the public health.

5.3 Premarket Tobacco Applications

If a new tobacco product meets the following…	FDA intends to enforce the FD&C Act as follows…
Is a non-combusted tobacco product marketed after the [effective date of part 1100 plus 72 months] and the manufacturer submits a 905(j) report for the product by [effective date of part 1100 plus 72 months].	FDA does not intend to initiate enforcement action against the product for failing to have an FDA marketing authorization unless and until FDA issues an order denying your substantial equivalence submission under 910(a)(2). If FDA issues such an order, FDA intends to enforce the premarket authorization requirements with respect to your product.
Is a non-combusted tobacco product marketed after the [effective date of part 1100 plus 72 months] and the manufacturer submits a PMTA report for the product by [effective date of part 1100 plus 72 months].	FDA does not intend to initiate enforcement action against the product for failing to have an FDA marketing authorization unless and until FDA issues an order denying your PMTA submission. If FDA issues such an order, FDA intends to enforce the premarket authorization requirements with respect to your product.
~~Is~~Is a combusted tobacco product marketed between February 15, 2007, and [effective date of part 1100 plus 24 months] and the manufacturer submits a 905(j) report for the product by [effective date of part 1100 plus 24 months].	FDA does not intend to initiate enforcement action against the product for failing to have an FDA marketing authorization unless and until FDA issues an order denying your substantial equivalence submission under 910(a)(2). If FDA issues such an order, FDA intends to enforce the premarket authorization requirements with respect to your product.
~~Is~~ Is a combusted product and marketed between February 15, 2007, and [effective date of part 1100 plus 24 months] and the manufacturer did not submit a 905(j) report for the product by [effective date of part 1100 plus 24 months] and has not filed a PMTA to obtained a marketing authorization order under section 910(c)(1)(A)(i).	FDA does not intend to initiate enforcement action against the product for failing to have an FDA marketing authorization until [effective date of part 1100 plus 24 months]. Thereafter, if no PMTA has been filed~~,~~ by the [effective date of part 110 plus 24 months], FDA intends to enforce the premarket authorization requirements with respect to the product.

If a new tobacco product meets the following…	FDA intends to enforce the FD&C Act as follows…
~~Would~~Is a combusted product and would be marketed on or after [effective date of part 1100 plus 24 months].	FDA intends to enforce the premarket authorization requirements with respect to the product.

Therefore, FDA is proposing a compliance period of 24 months for combusted tobacco products after the effective date of this rule and 72 months for non-combusted tobacco products—during which time FDA would not intend to initiate enforcement against the product on the market for failing to have a marketing order from FDA. Under FDA's proposal, FDA would not intend to initiate enforcement action for failure to have a marketing authorization against proposed deemed tobacco products first introduced or delivered for introduction into interstate commerce for commercial distribution after February 15, 2007, and prior to the 905(j) proposed compliance date (i.e., effective date plus 24 months~~)~~, only, provided a 905(j) report is submitted no later than the proposed compliance date, and FDA has not issued an order finding the tobacco product to be not substantially equivalent. In these cases, the Agency would not intend to initiate enforcement action against the tobacco product on the market for failure to have a marketing authorization unless and until FDA issues an order that the tobacco product is not substantially equivalent to the predicate tobacco product (section 910(a)(2)(A) of the FD&C Act). FDA would consider taking different or additional actions if it believes particular circumstances warrant them. FDA would also consider revising its compliance policy should the Agency find that doing so is warranted, such as to better protect the public health.

6 Evidence Summary: Consumers lack necessary information, and much of what they *think* they know is wrong

6.1 Data on misperceptions of relative lack of harm from other forms of nicotine consumption (NRT, SLT, e-cigarettes)

6.1.1 Viscusi (in press)

Drawing on evidence from a new nationally representative survey, this article examines several measures of risk beliefs for e-cigarettes. For both lung cancer mortality risks and total smoking mortality risks, respondents believe that e-cigarettes pose risks that are lower than the risks of conventional tobacco cigarettes. However, people greatly overestimate the risk levels of e-cigarettes compared to the actual risk levels. Risk beliefs for conventional cigarettes receive at least a two-thirds informational weight in the formation of e-cigarette risk beliefs. Public perceptions of nicotine levels of e-cigarettes are closer to the beliefs for conventional cigarettes than are their health risk perceptions. Consumers' desired uses of e-cigarettes are more strongly related to health risk perceptions than perceived e-cigarette nicotine levels. The overestimation of e-cigarette risks establishes a potential role for informational policies.

6.1.2 Kiviniemi & Kozlowski (2015)

Background: Tobacco products differ in their relative health harms. The need for educating consumers about such harms is growing as different tobacco products enter the marketplace and as the FDA moves to regulate and educate the public about different products. However, little is known about the patterns of the public's knowledge of relative harms.

Methods: Data were analyzed from the Health Information National Trends Survey (HINTS) 4 Cycle 2, a population representative survey of US adults conducted between October 2012 and January 2013 (N = 3630). Participants reported their perceptions of the relative risks of e-cigarettes, smokeless tobacco, and different types of cigarettes compared to "traditional" cigarettes. Relative risk perceptions for each product type, as well as the consistency and accuracy of harm reduction beliefs, were analyzed.

Results: About 65 % of the respondents accurately reported that no cigarettes were less harmful than any others. Slightly more than half of US adults perceived e-cigarettes to be safer than regular cigarettes, a belief in line with current scientific evidence. By contrast, only 9 % of respondents perceived some smokeless tobacco products to be safer, a belief strongly supported by the evidence. Only 3.5 % of respondents had patterns of relative risk perceptions in line with current scientific evidence for all three modalities.

Conclusions: The discrepancy between current evidence and public perceptions of relative risk of various tobacco/nicotine products was marked; for most tobacco types, a large proportion of the population held inaccurate harm reduction beliefs. Although there was substantial awareness that no cigarettes were safer than any other cigarettes, there could be benefits from increasing the percentage of the public that appreciates this fact, especially among current smokers. Given the potential benefits of tobacco risk reduction strategies, public health education efforts to increase understanding of basic harm reduction principles are needed to address these misperceptions.

6.1.3 Brose et al. (2015)

Introduction: Media presentations of e-cigarettes may affect perception of the devices which may influence use.

Objectives: To assess in a cohort of past-year smokers (1) if perceived harm of e-cigarettes relative to cigarettes changed over time, (2) predictors of perceived relative harm, (3) if perceived relative harm predicted subsequent e-cigarette use among never-users.

Methods: Longitudinal web-based survey of a general population sample of British smokers and ex-smokers, waves in 2012 (n = 4553), 2013 and 2014 (44%, 31% response rate, respectively). Changes overtime were assessed using Friedman and McNemar tests, n = 1204. Perceived relative harm at wave 3 was regressed onto perceived relative harm at waves 1 and 2, while adjusting for socio-demographics and change in smoking and e-cigarette status, n = 1204. Wave 2 e-cigarette use among 1588 wave 1never-users was regressed onto wave 1 socio-demographics, smoking status and perceived relative harm.

Results: Perceived relative harm changed (x^2= 20.67, p < 0.001); the proportion perceiving e-cigarettes to be less harmful than cigarettes decreased from 2013 to 2014 (x^2= 16.55, p < 0.001). Previous perceptionof e-cigarettes as less harmful, having tried e-cigarettes and having stopped smoking between waves predicted perceiving e-cigarettes as less harmful than cigarettes. Perceiving e-cigarettes to be less harmful than cigarettes predicted subsequent use, adjusting for other characteristics (OR = 1.39; 95% CI: 1.08–1.80, p = 0.011).

Conclusion: Among a cohort of smokers and ex-smokers, accurately perceiving e-cigarettes as less harmful than smoking predicted subsequent e-cigarette use in never-users; this perception declined over time. Clear information on the relative harm of cigarettes and e-cigarettes is needed.

6.1.4 Silla et al. (2014)

Background: Smokers who are unwilling or unable to quit smoking may benefit from using nicotine replacement therapy (NRT) for harm reduction. This may include the partial or complete substitution of cigarettes with NRT. A taxonomy of the characteristics of those using NRT for harm reduction would be helpful in tailoring advice and treatment. Although attempts to categorize those using NRT for harm reduction have been made, these have largely been based on quantitative data. In order to provide further in-depth exploration of views, beliefs and experiences, the current study probed issues surrounding NRT and harm reduction qualitatively to better understand barriers and facilitators to this approach.

Methods: Three groups of participants (n = 15) were recruited from a student sample: current smokers with a history of NRT use, smokers without a history of NRT use, and ex-smokers with a history of NRT use. Participants were asked about their demographic characteristics, smoking behaviours, intention and perceived ability to quit smoking, awareness and use of NRT, beliefs about the health consequences of using NRT, and the safety and efficacy of NRT, using semi-structured telephone interviews.

Results: Twenty-four themes were identified; these themes were clustered into three main issues of cross-cutting themes: attitudes towards smoking and motivation to quit; smoking reduction and quit attempts; and beliefs, use and concerns about NRT. Those with a history of NRT use were more motivated and engaged with the quitting process than non-users. However, irrespective of smoking status and past NRT use, all participants showed misperceptions about NRT, such as the health consequences associated with NRT use.

Conclusions: NRT users are more motivated to quit smoking than non-users and are more likely to employ techniques to assist their cessation attempts. The majority of smokers have misperceptions regarding the safety and efficacy of NRT which may act as a barrier to its usage.

6.1.5 Ferguson et al. (2011)

Aim: Previous studies have reported that smokers who are misinformed about the safety of Nicotine Replacement Therapy (NRT) are less likely to report using it. In this

study, we examined whether providing information that counters these concerns might impact on intentions to use NRT.

Participants: 900 smokers recruited from a market research database.

Design and setting: Participants completed an online survey that asked about their views about NRT. Smokers with safety and efficacy concerns were queried to determine whether accurate information might increase their interest in using NRT.

Findings: Misperceptions of NRT safety were common: 93% of smokers did not know that smoking while wearing the nicotine patch does not cause heart attacks; 76% that nicotine gum/lozenge are not as addictive as cigarettes; and 69% that NRT products are not as dangerous as cigarettes. Over half of the smokers with misperceptions reported that they would be more likely to use NRT to help them quit smoking if they were exposed to information correcting their concerns (53%, 58% and 66%, respectively, for each of the misperceptions).

Conclusions: These data suggest that while a sizeable proportion of smokers are still misinformed about the safety of NRT, misinformed smokers would increase consideration of NRT if these misperceptions are addressed by corrective information.

6.1.6 Shiffman et al. (2008)

Aim Nicotine replacement therapy (NRT) is effective for smoking cessation, but most smokers try to quit without using it. We examined the impact of misperceptions of NRT safety and efficacy on its use. **Design and participants** A total of 3203 current and former US smokers completed a national mail-out survey of issues and attitudes related to smoking cessation. **Findings** Two-thirds (66%) of respondents either agreed that 'Stop-smoking products with nicotine are just as harmful as cigarettes' or were unsure whether the statement was true. These respondents were less likely to have used NRT in the past [30% versus 49%; odds ratio (OR) = 0.45, 95% confidence interval (CI): 0.39–0.53] and less likely to consider using NRT during future quit attempts (40% versus 53%; OR = 0.60, 95% CI = 0.51–0.71). Additionally, of the respondents who had used nicotine gum in the past 12 months (n = 407), those who had concerns about the safety of NRT reported using fewer pieces of gum per day during treatment (six versus eight pieces/day; $P < 0.05$), and were less likely to report that they used the gum for greater than 4 weeks (28.5% versus 46.8%; OR = 0.45, 95% CI: 0.27–0.76). A large proportion of the respondents also stated that they did not believe NRT to be efficacious. **Conclusions** The findings suggest that many smokers are misinformed about the health risks of NRT and that these misperceptions impede not only the adoption of NRT but also compliance during treatment. Misperception of NRT safety is one barrier to effective use of NRT and probably reduces success in quitting.

6.1.7 Mooney et al. (2006)

Nicotine replacement therapies (NRTs) represent an effective means of promoting smoking cessation, but they remain underutilized. Negative attitudes and false beliefs about nicotine and nicotine replacement may cause NRT underutilization. In a randomized, controlled, single-blind study of nicotine gum, 97 smokers were assessed

on their attitudes and knowledge about nicotine, nicotine replacement, and smoking cessation therapy. Information from these self-report measures was used in an intervention that provided tailored, brief feedback to promote positive attitudes and accurate knowledge about NRT. Considerable variability in pretreatment attitudes and knowledge was observed across individuals. Moreover, attitudes and knowledge showed a consistent pattern of intercorrelation and were systematically related to smoking characteristics (e.g., prior use of NRT, nicotine dependence, treatment completion). The brief feedback intervention led to a significant global elevation in attitudes about nicotine, NRT, and assisted cessation but not knowledge about nicotine. Changes in attitudes and knowledge were not significantly related to gum use or smoking cessation. Recommendations for the appropriate application of brief feedback are offered.

6.1.8 Bansal et al. (2004)

This study assessed smokers' beliefs about nicotine and the safety of nicotine medications and examined how these beliefs influence the use of nicotine medications. The data for this paper came from a nationally representative, random-digit-dialed telephone survey of 1,046 adults (18 years of age and older) current cigarette smokers conducted between May and September 2001. Respondents were questioned about their use of stop smoking medications, beliefs about nicotine, and the safety/efficacy of nicotine medications. Nearly all adult smokers in our survey had heard of nicotine patches (97%) or gum (94%), with lower levels of awareness reported for the nicotine inhaler (41%), and nasal spray (9%). Thirty-eight percent of smokers had previously used nicotine medications, with the nicotine patch being the most commonly used medication. The data reveal that most smokers are misinformed about the health risks of nicotine and the safety/efficacy of nicotine medications. Approximately half incorrectly reported that the reduction in nicotine in cigarettes has made cigarettes less dangerous to health and only one-third correctly reported that nicotine patches were less likely to cause a heart attack than smoking cigarettes. Smokers who were more knowledgeable about the health risks of nicotine and the safety and efficacy of nicotine medications were more likely to report past use of nicotine medications. Misperceptions about the health risks of nicotine and the safety/efficacy of nicotine medications may discourage some smokers from considering the use of these medications to help them stop smoking.

6.2 Data indicating that correcting misperceptions changes consumers' intentions

6.2.1 Rousu et al. (2014)

Objectives

This study explored the relationship between product trials and consumer demand for alternative nicotine products (ANP).

Methods

An experimental auction was conducted with 258 adult smokers, wherein participants were randomly assigned to one of four experimental conditions. The participants

received the opportunity to try, but did not have to accept, one of three relatively novel ST products (i.e., snus, dissolvable tobacco, or medicinal nicotine), or they were placed into a control group (i.e., no trial). All the participants then bid on all three of these products, as well as on cigarettes. We assessed interest in using ANP based on both trial of the product and bids placed for the products in the experimental auction.

Results
Fewer smokers were willing to try snus (44 %) than dissolvable tobacco (64 %) or medicine nicotine (68 %). For snus, we find modest evidence suggesting that willingness to try is associated with greater demand for the product. For dissolvable tobacco or medicinal nicotine, we find no evidence that those who accept the product trial have higher demand for the product.

Conclusions
Free trials of a novel ANP were not strongly associated with product demand, as assessed by willingness to pay. Given the debate over the potential for ANP to reduce the harm from smoking, these results are important in understanding the impact of free trial offers on adoption of ST product as a strategy to reduce harm from tobacco use.

6.2.2 Ferguson et al. (2011)

Aim: Previous studies have reported that smokers who are misinformed about the safety of Nicotine Replacement Therapy (NRT) are less likely to report using it. In this study, we examined whether providing information that counters these concerns might impact on intentions to use NRT.

Participants: 900 smokers recruited from a market research database.

Design and setting: Participants completed an online survey that asked about their views about NRT. Smokers with safety and efficacy concerns were queried to determine whether accurate information might increase their interest in using NRT.

Findings: Misperceptions of NRT safety were common: 93% of smokers did not know that smoking while wearing the nicotine patch does not cause heart attacks; 76% that nicotine gum/lozenge are not as addictive as cigarettes; and 69% that NRT products are not as dangerous as cigarettes. Over half of the smokers with misperceptions reported that they would be more likely to use NRT to help them quit smoking if they were exposed to information correcting their concerns (53%, 58% and 66%, respectively, for each of the misperceptions).

Conclusions: These data suggest that while a sizeable proportion of smokers are still misinformed about the safety of NRT, misinformed smokers would increase consideration of NRT if these misperceptions are addressed by corrective information.

6.2.3 Blake et al. (2015)

Objectives: To assess adult smokers' exposure to information about e-cigarettes, whether exposure independently predicts e-cigarette use behavior and perceptions

about addiction and reduced harm, and whether the effect of information exposure on e-cigarette use is mediated by reduced harm perceptions.

Methods: Data were collected using a representative online panel of current adult cigarette smokers (N = 2254). Multivariable logistic regression was employed to assess whether information exposure predicted e-cigarette use and perceptions of reduced harm, and a mediation model was employed to test whether harm perceptions mediated the influence of information exposure on e-cigarette use.

Results: Forty percent of respondents reported seeing, hearing, or reading about e-cigarettes in the media "a lot of times," with television and point-of-sale being the most common channels of exposure. Those reporting a lot of exposure were 40% more likely than those reporting low or no exposure to say that using e-cigarettes is "not at all harmful" to a person's health (OR=1.43, CI=1.006, 2.050) and were 40% more likely to say they use e-cigarettes every day or some days (OR=1.406, CI=1.034, 1.912).

Conclusions: Exposure to information about e-cigarettes is associated with reduced harm perceptions and e-cigarette use.

7 References

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August 8, 2014

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Re: Deeming Tobacco Products To Be Subject to the Federal Food, Drug, and Cosmetic Act, as Amended by the Family Smoking Prevention and Tobacco Control Act; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products; Proposed Rule (Docket No. FDA–2014–N–0189)

Dear Commissioner Hamburg:

We write as public health professionals who have worked on tobacco and public health issues with the federal government, academia, health voluntary organizations, and as consultants to the private sector. Our consulting firm provides services for a range of companies, including for GlaxoSmithKline Consumer Healthcare on their stop-smoking medications (Nicorette and NicoDermCQ in the US) and for NJOY, Inc., a developer and marketer of electronic nicotine delivery systems. Some of us (JMP, JGG, JEH, SS) also are members in a limited liability corporation that owns intellectual property for an as-yet not-commercialized nicotine gum. These comments, however, reflect our own views exclusively and with them we are representing no one but the undersigned.

The proposed rule, at a strategic and regulatory policy level, sets a positive tone and direction that we believe holds the promise to minimize, and eventually to eliminate, the harm caused by the use of tobacco products within our lifetimes. The ongoing development, implementation, and subsequent refinement of a comprehensive regulatory framework for all nicotine-containing products by FDA will not be simple, easy, nor linear—but it is vitally important to achieve the overarching goal of empowering millions of Americans to not surrender tens of millions of life-years lost due to the inhalation of combusted tobacco smoke. We draw some of our inspiration from the Tobacco End Game Strategies and Projections described in Chapters 15 and 16 of the 2014 Surgeon General's Report (SGR), the Tobacco Endgame conference convened by Kenneth Warner (Warner, 2013), the Strategic Dialog effort and report that were co-chaired and co-authored by Mitch Zeller and Dorothy Hatsukami (Zeller and Hatsukami, 2009) and the work of Dr. Walton Sumner who carefully modeled the massive potential health benefits from adopting thoughtful nicotine product regulation (Sumner 2003; 2005). You have already received many comments on very specific

aspects of tobacco regulation. In this comment we will focus on what we believe should be the overarching goals and approach to tobacco product regulation.

Central to the very notion of product regulation being possible is the awareness and acceptance that there is large variability across "nicotine delivery systems" (NDS) including traditional and novel tobacco products and nicotine replacement therapy (NRT) medications on characteristics that influence their impact on public health. This has been referred to by Mr. Zeller and others as a "continuum of risk." A core premise of the Family Smoking Prevention and Tobacco Control Act and FDA tobacco regulation is that NDS do vary widely in toxicity and addictiveness, that determinants of toxicity and addictiveness can and should be regulated to benefit public health, in part to reduce the use of the most toxic and addictive products.

It is now well accepted that there are massive differences in inherent toxicities of NDSs with combusted tobacco products being by far the most harmful at the individual and population levels (SGR, 2014; FDA Proposed Deeming Rule, 2014). This variability makes product regulation not only possible, but highlights the promise it can hold for effective tobacco control.

Following on the emerging work from Dr. David Abrams and colleagues of the Schroeder Institute for Tobacco Research and Policy Studies at Legacy (see link for presentation of "A Strategic Agenda for E-Cig Research"), we would recommend that all NDSs be evaluated on three separate but related axes as part of the Triple Continua Framework (TCF). Dr. Abrams has described axes that map very closely on to the CTP's announced three areas for consideration of product standards: toxicity, addiction, and appeal. We believe that these are critically important, but have sought to augment the utility of this framework by tweaking the description of the three axes:

1. Inherent toxicity – how harmful is the use of the product, both to users and non-users?

2. Nicotine use experience – this axis includes concepts such as addictiveness and abuse liability, but we also add broader notions such as satisfaction and reward that can largely be assessed with the behavioral question of: how difficult is it for a user who chooses to stop use to completely stop use of a NDS?

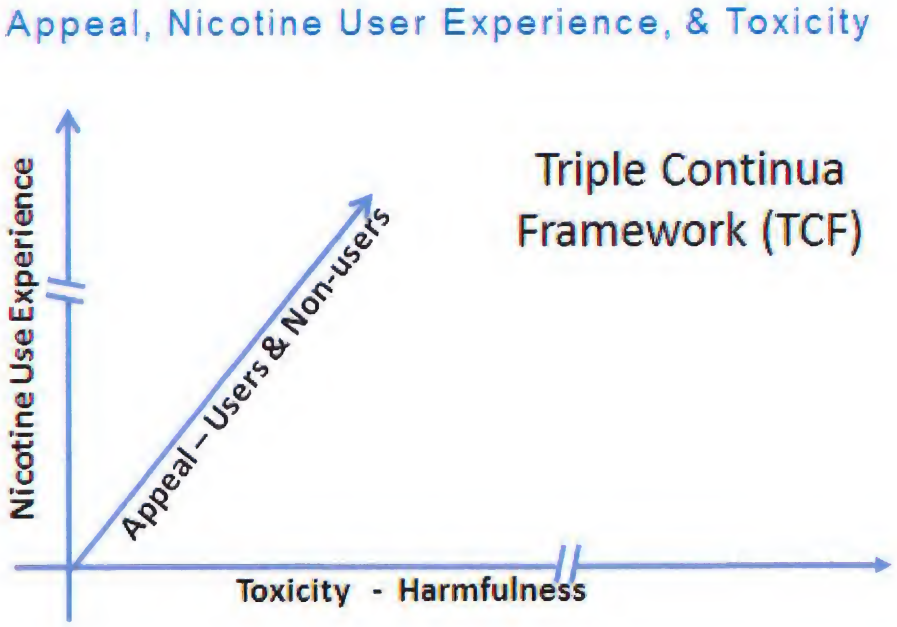
3. Appeal – how attractive and alluring is a product (to never users, experimenters, and established users)? Importantly, while appeal to persons not using traditional tobacco products would be regarded with concern, appeal to tobacco users is essential to ensure adoption and "reach" of products that are expected to have a public health benefit.

Using the three TCF axes above, we believe it is possible to rate NDSs relative to each other and to create a standardized approach for regulating all NDSs. We are not asserting that the available science yet allows precise and accurate ratings of every product on all three axes (or even necessarily determining that the axes would use

linear or even logarithmic scales, as indicated by the axes breaks), but we believe that current evidence clearly supports the conceptualization of the opportunity with this framework. Further, we are confident that the development and dissemination of further data-generation will allow ever greater refinement and precision with these ratings.

In the two graphics below, modified and used with permission from Dr. David Abrams, one can see graphically how such an evaluation would proceed. The X axis represents the inherent toxicity (predominantly the toxicity for users) of the product, the Y axis shows the nicotine user experience, and the Z axis is the appeal of the product.

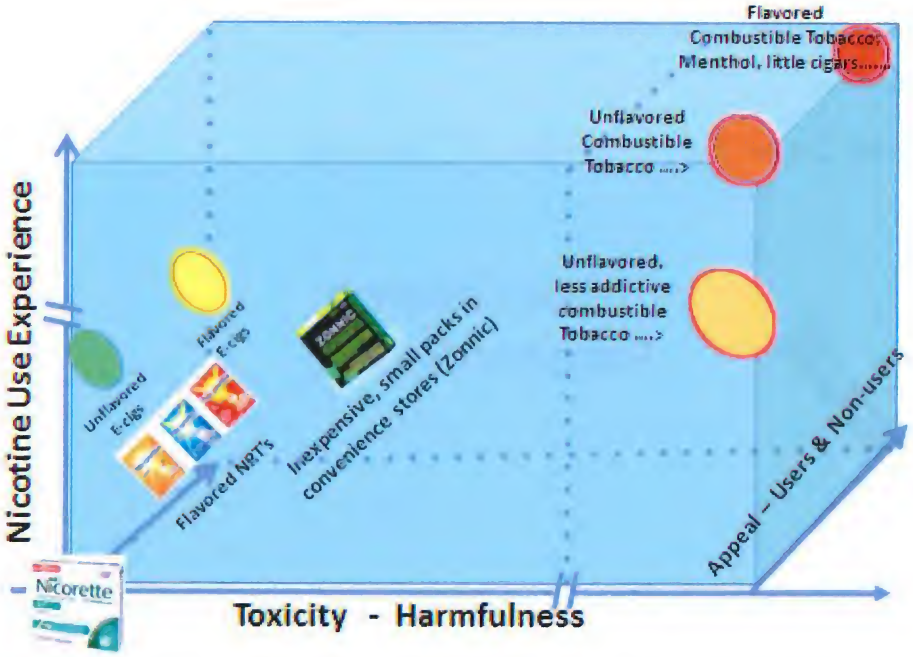
Figure 1: Triple Continua Framework (Schematic)



In the second figure (see Figure 2), we have included a range of example NDSs to flesh out this three-dimensional space. The top, back, right corner is defined by combustion tobacco products (combustible cigarettes, predominantly), which sets the maximum rating for all three scales: combustible cigarettes are the most harmful, most addictive, and most appealing tobacco products. In the opposite corner from combustion products is placed mainstream nicotine medications (NM), the lowest in toxicity, nicotine use experience and appeal. We postulate that a variety of flavors, and smaller packages with less medicinal positioning (e.g., positioned less as treatments for a disease and more as a conventional consumer product—see this report from the Consumer Demand Roundtable project for more details), may enhance the appeal of NM without increasing its toxicity. We also assume that electronic nicotine delivery systems (ENDS) are broadly similar to NM in terms of inherent toxicity to existing users, but they appear, based on consumer adoption and use, to offer both a more satisfying user experience

and are more appealing than NM. This assertion is consistent with the very recent and comprehensive review by Hajek et al (2014). Key relevant research is also included in the review of ENDS related literature by FDA Center for Tobacco Products Scientists as published in a special issue of Tobacco Control (Vol. 23, May, 2014) In addition, we believe that the available data are consistent with the assertion that flavors for ENDS enhance both their appeal and the user experience.

Figure 2: Triple Continua Framework (Populated)



Back to the "high-toxicity" right-hand section of the chart, we envision a future where, through product-regulation tools such as product standards, including reduction in nicotine content, the appeal and addictiveness of combustion products are reduced (and thus those shapes move "forward" and "down").

Comprehensive tobacco control efforts must strive to achieve and balance the goals of reducing the likelihood that any current non-smoker (regardless of age) becomes a cigarette smoker, and helping tobacco users – combustion tobacco users in particular – to reduce their exposure to tobacco toxins as quickly and substantially as possible, ideally completely eliminating their use of combusted tobacco products and exposure to tobacco smoke.

In sum, we argue that it is essential to approach the regulation of all NDSs comprehensively with balanced efforts to contribute to the most rapid reduction possible of exposure to the largest preventable public health hazards in our nation: combusted tobacco product emissions. Presently, combustion products, cigarettes in particular, are

the most widely used, and are the most attractive and addictive, whereas less toxic substitute products such as e-cigarettes are less attractive and less addictive. Balanced regulation that begins to reverse this quandary by making combustion products less attractive and less addictive, while enabling noncombustion products to be adequately attractive and capable of nicotine delivery to facilitate their substitution for cigarettes is essential to foster the mass migration from combusted tobacco to noncombustion products. With the combination of acceptable, legal, and regulated substitutes for combustion cigarettes, which are essentially inferior and defective goods (facing ever increasing regulation), the public health impact of tobacco use could be minimized.

Sincerely,

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